# General

## Guideline Title

Targeted therapy for locally advanced unresectable or metastatic medullary thyroid carcinoma.

## Bibliographic Source(s)

Alberta Provincial Endocrine Tumour Team. Targeted therapy for locally advanced unresectable or metastatic medullary thyroid carcinoma. Edmonton (Alberta): CancerControl Alberta; 2012 Nov. 7 p. (Clinical practice guideline; no. ENDO-002). [23 references]

## Guideline Status

This is the current release of the guideline.

# Recommendations

## Major Recommendations

1. Vandetanib has been shown to slow symptomatic or anatomic progression (versus placebo) in patients with progressive medullary thyroid carcinoma. Therefore, vandetanib is recommended for patients with symptomatic or progressive medullary thyroid carcinoma with unresectable locally advanced or metastatic disease.
2. Vandetanib should be given at a dose of 300 mg, orally, daily.

## Clinical Algorithm(s)

None provided

# Scope

## Disease/Condition(s)

Locally advanced unresectable or metastatic medullary thyroid carcinoma

## Guideline Category

Management

Treatment

## Clinical Specialty

Endocrinology

Oncology

## Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

## Guideline Objective(s)

To provide evidence-based recommendations on the use of vandetanib for medullary thyroid carcinoma and to define which patients are acceptable candidates for treatment with this agent

## Target Population

Patients diagnosed with locally advanced unresectable or metastatic medullary thyroid carcinoma

## Interventions and Practices Considered

Vandetanib

## Major Outcomes Considered

- Survival rates (5-year, progression-free)
- Response rates
- Adverse events

# Methodology

## Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Questions

- Is vandetanib more effective than placebo in delaying progression among patients with medullary thyroid carcinoma? If so, what selection criteria should be considered when identifying patients who are appropriate for treatment with vandetanib?
- What is the appropriate dosing regimen for vandetanib?

Search Strategy

The Medline database was searched (1965 through 2012 March) for relevant publications using the following search terms: *vandetanib* AND *medullary thyroid*. Results were limited to randomized controlled trials and phase II-III clinical trials. In addition, the National Guideline Clearinghouse database was searched (2006 through 2012 March) for existing guidelines and the American Society of Clinical Oncology (ASCO) meeting abstracts database was searched (2009 through 2012 March) for relevant abstracts. Finally, chemotherapy protocols for vandetanib were searched on the Cancer Care Ontario (CCO) and British Columbia Cancer Agency (BCCA) websites.

## Number of Source Documents

A total of three citations were returned from Medline, all of which were relevant, and one American Society of Clinical Oncology (ASCO) abstract was selected.

## Methods Used to Assess the Quality and Strength of the Evidence

Not stated

## Rating Scheme for the Strength of the Evidence

Not applicable

## Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial Endocrine Tumour Team and a Knowledge Management (KM) Specialist from the Guideline Utilization Resource Unit (GURU). A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, GURU does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Evidence is summarized in the table in Appendix B in the original guideline document.

## Methods Used to Formulate the Recommendations

Expert Consensus

## Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

## Rating Scheme for the Strength of the Recommendations

Not applicable

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Internal Peer Review

## Description of Method of Guideline Validation

This guideline was reviewed and endorsed by the Alberta Provincial Endocrine Tumour Team.

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management (KM) Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

# Evidence Supporting the Recommendations

## Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

# Benefits/Harms of Implementing the Guideline Recommendations

## Potential Benefits

### Potential Benefits

Appropriately targeted therapy for locally advanced unresectable or metastatic medullary thyroid carcinoma

### Potential Harms

The most frequently reported adverse events (any grade) associated with vandetanib are diarrhea (56% versus 26% placebo), rash (45% vs. 11% placebo), nausea (33% versus 16% placebo), hypertension (32% versus 5% placebo), and headache (26% versus 9% placebo). The most frequent grade 3 or higher events were diarrhea (11% versus 2% placebo), hypertension (9% versus 0% placebo), and electrocardiogram (ECG) QT prolonged (8% versus 1% placebo). Patients, especially those with a history of cardiovascular disorders, for whom vandetanib is planned should be monitored closely by physicians for cardiovascular events.

Refer to Appendix B in the original guideline document for a complete listing of adverse events reported in published clinical trials.

## Qualifying Statements

### Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial Endocrine Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

## Implementation of the Guideline

### Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

## Institute of Medicine (IOM) National Healthcare Quality Report Categories

### IOM Care Need

Getting Better

Living with Illness

### IOM Domain

Effectiveness

## Identifying Information and Availability

### Bibliographic Source(s)

Alberta Provincial Endocrine Tumour Team. Targeted therapy for locally advanced unresectable or metastatic medullary thyroid carcinoma. Edmonton (Alberta): CancerControl Alberta; 2012 Nov. 7 p. (Clinical practice guideline; no. ENDO-002). [23 references]

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2012 Nov

## Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

## Source(s) of Funding

CancerControl Alberta

## Guideline Committee

Alberta Provincial Endocrine Tumour Team

## Composition of Group That Authored the Guideline

Members of the Alberta Provincial Endocrine Tumour Team include medical oncologists, endocrinologists, radiation oncologists, surgeons, and nurses.

## Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial Endocrine Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial Endocrine Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

## Guideline Status

This is the current release of the guideline.

## Guideline Availability

Electronic copies: Available from the Alberta Health Services Web site .

## Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Electronic copies: Available from the Alberta Health Services Web site .

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on August 12, 2014. The information was verified by the guideline developer on September 25, 2014.

## Copyright Statement



# Disclaimer

## NGC Disclaimer